

Table 37: Opioid Analgesics and Tramadol (also see prescribing information)

Class or Drug	Mechanism of Action	Clinical Comments
<ul style="list-style-type: none"> NRTIs Dolutegravir (DTG) Bictegravir (BIC) Cabotegravir (CAB) Raltegravir (RAL) Rilpivirine (RPV) Etravirine (ETR) Doravirine (DOR) Fostemsavir (FTR) 	No significant interactions reported.	No dose adjustments are required.
Elvitegravir (EVG), boosted	<ul style="list-style-type: none"> Opioid analgesics: Complex mechanisms of metabolism and formation of both active and inactive metabolites create interactions of unclear significance between these drugs and boosted EVG. Tramadol: Tramadol exposure is increased with CYP3A inhibition, but this reduces conversion to more potent active metabolite seen when tramadol is metabolized by CYP2D6. 	<ul style="list-style-type: none"> Opioid analgesics: Monitor for signs of opiate toxicity and analgesic effect and dose these analgesics accordingly. Tramadol: When tramadol is given with COBI or RTV, monitoring for tramadol-related adverse effects and analgesic effect may be required as clinically indicated; adjust tramadol dosage if needed.
Boosted PIs	<ul style="list-style-type: none"> Opioid analgesics: Complex mechanisms of metabolism and formation of both active and inactive metabolites create interactions of unclear significance between these drugs and boosted PIs. Tramadol: Tramadol exposure is increased with CYP3A inhibition, but this reduces conversion to more potent active metabolite seen when tramadol is metabolized by CYP2D6. 	<ul style="list-style-type: none"> Opioid analgesics: Monitor for signs of opiate toxicity and analgesic effect; dose these analgesics accordingly. Tramadol: When tramadol is given with COBI or RTV, monitoring for tramadol-related adverse effects and analgesic effect may be required as clinically indicated; adjust tramadol dosage if needed.
Efavirenz (EFV)	<ul style="list-style-type: none"> Morphine, hydromorphone: Metabolism could be reduced by EFV. Oxycodone may be metabolized faster to inactive metabolite by EFV. Meperidine: Coadministration can potentially increase amount of neurotoxic metabolite, thereby increasing seizure risk. Tramadol: EFV may reduce tramadol concentration without affecting pathway that increases development of more potent active metabolites. 	<ul style="list-style-type: none"> Morphine, hydromorphone: Monitor for signs of opiate toxicity when using with EFV. Oxycodone: Dose adjustment of oxycodone may be required when dosing with EFV. Meperidine: If possible, avoid concomitant use; use alternative opiate pain medication or ARV. Tramadol: When given with tramadol, a priori dose adjustments are necessary.
Lenacapavir (LEN)	Moderate inhibition of CYP3A4 potentially increases opioid levels.	<ul style="list-style-type: none"> Monitor for therapeutic effects and adverse reactions associated with CYP3A-metabolized opioid analgesics, including potentially fatal respiratory depression. Tramadol: Consider tramadol dose reduction with concomitant use.

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Abbreviations: ARV, antiretroviral; COBI, cobicistat; CYP, cytochrome P450; NRTI, nucleoside reverse transcriptase inhibitor; PI, protease inhibitor; RTV, ritonavir.		